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**Original Article**

# Pentraxin-3, endothelin-1, some biochemical parameters and hematology in bovine respiratory disease complex

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## Abstract

**Background:** Infectious bovine respiratory disease complex (BRDC) is one of the world's major livestock problems. **Aims:** The study aimed to determine the diagnostic importance of pentraxin-3, endothelin-1, clinical biochemistry, and hematological parameters in infectious BRDC. **Methods:** Animals in this study were Simmental breed, 1-7 years old, untreated, and healthy and BRDC cattle (40 cattle with BRDC in the disease group, and 10 healthy cattle in the control group). Clinical findings such as general posture, respiratory rate per minute, rectal temperature, heart rate per minute, and mental posture of the diseased cattle were recorded. Blood samples were taken from the jugular vein only once from all cattle. Complete blood count from blood samples was measured in an automatic complete blood count device, biochemical parameters in an autoanalyzer, and pentraxin-3 and endothelin-1 were measured by ELISA method. **Results:** Rectal temperature, respiratory and pulse rates per minute, total leukocyte count, gamma-glutamyl transferase, urea, total bilirubin, lactate dehydrogenase, creatine kinase, pentraxin-3 and endothelin-1 concentrations were found to be statistically higher in BRDC group than those in the control group ($P<0.001$). **Conclusion:** Pentraxin-3 and endothelin-1 levels were statistically significantly higher in the BRDC group compared to the control group. As a result, pentraxin-3 and endothelin-1 were found to be diagnostically important in cattle diagnosed with BRDC.

**Key words:** BRDC, Cattle, Endothelin-1, Hematology, Pentraxin-3

## Introduction

The infectious bovine respiratory disease complex (BRDC) is one of the crucial problems in livestock worldwide, which is caused by many viral and bacterial factors and may lead to death (Edwards, 2010). BRDC is a common and economically important disease in today's livestock industry (Guterbock, 2014). It is shown as an important cause of death in both beef cattle and dairy cattle industries (Miles, 2009; Patric, 2009). The immune system, herd management, environmental factors, and infectious factors are shown as important factors in causing disease in cattle by BRDC (Panciera and Confer, 2010; Taylor *et al*., 2010). The risk factors of the disease include weaning, surgical procedures applied during weaning, lack of natural or vaccine immunities, changes in nutrition, other infections, and climatic conditions coinciding (Taylor *et al*., 2010; Hilton, 2014). BRDC is a multifactorial disease of the lower respiratory tract of cattle resulting in bronchopneumonia. Typical viral pathogens are infectious bovine rhinotracheitis virus (IBR), bovine herpes virus-1 (BHV-1), parainfluenza type 3 virus (BPI-3), and bovine respiratory syncytial virus (BRSV). The involved bacteria are *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni*, and *Mycoplasma bovis* (Hilton, 2014). Basic immune

mechanisms such as mucus production and ciliary epithelial movement actively inhibit the colonization of pathogens in the lower respiratory tract. In BRDC, this homeostatic balance in the upper tract results in colonizing infective agents in the lower tract (McMullen *et al*., 2020; Bell *et al*., 2021). Pentraxin-3 is an acute-phase protein similar in structure and function to C-reactive protein. Pentraxin-3 is released from macrophages, dendritic cells, leukocytes, and endothelial cells during the inflammatory response (Libby *et al*., 2009). Pentraxin-3 more clearly reflects the inflammatory state when compared with the classical pentraxins, C-reactive protein, and serum amyloid A. Therefore, pentraxin-3 may be an appropriate independent indicator of disease activity (Fujita *et al*., 2012). Pentraxin-3 recognizes and binds to many pathogens, activates complement, and clears apoptotic and necrotic cells. In addition, pentraxin-3 has an important protective role in bacterial lung inflammation and disease (Townsend and Singh, 2021). Endothelin-1 is a very potent vasoconstrictor released by endothelial cells. In endotoxemias, pre-pro-endothelin-1 is released from the heart and lungs, and it increases in direct proportion to the mortality rates of the diseases (Tschaikowsky *et al*., 2000; Shah, 2007; Sonmezer and Tulek, 2015). Endothelin-1 is a 21 amino acid peptide with diverse biological activity associated with numerous diseases. Endothelin-1 is an inflammatory mediator that may play a key role in acute and chronic airways, pulmonary circulation, and inflammatory lung diseases (Fagan *et al*., 2001). Pentraxin-3 has been studied in veterinary medicine in a limited number of bovine respiratory diseases. Pentraxin-3 reflects the inflammatory state more clearly than classical pentraxins. Endothelin-1 is an inflammatory mediator that may play a key role in inflammatory lung diseases. The present study aimed to determine the diagnostic importance of pentraxin-3, endothelin-1, clinical biochemistry, and hematological parameters in BRDC in cattle. In addition, the clinical significance of pentraxin-3 and endothelin-1 was tried to be revealed.

## Materials and Methods

This study was carried out after approval from the Local Ethics Committee of Kafkas University (KAU-HADYEK/2021-149 and 2022-059), Kars, Turkey.

### Animals

Animals in his study were Simmental breed and crossbreed, 1-7 years old, untreated, and diagnosed with BRDC (40 cattle with BRDC in the disease group, and 10 healthy cattle in the control group). Sick cattle were included in the study as a result of clinical and physical examination findings, auscultation examination, radiographic findings, and hematological and laboratory examinations. Cattle with anorexia, dyspnea, cough, nasal discharge ranging from serous to mucopurulent, and hard vesicular and pathological sounds on auscultation were considered in the disease group. The study did not include animals with clinically determined diseases other than respiratory system disease. All sick animals were obtained from family-type cattle farms in our region that were referred to Kafkas University Faculty of Veterinary Animal Hospital, Kars, Turkey. The majority (90%) of the cattle in disease and control groups were between 2-4 years of age, with a mean age of 3.5 years old. The disease duration of the sick cattle was recorded in line with the anamnesis information obtained from the patient owners. Consideringly, 24 cattle had complaints of illness for 1-7 days, and 16 cattle had complaints of illness for a week or more. Of the cattle with BRDC, eight were male, and 32 were female. In the healthy group, two were male, and eight were female. It was determined that 50% of the female animals were late pregnant at six months and above. The cattle in the control group were selected similarly to the diseased group. A 10 ml blood sample was taken once from the jugular vein of all cattle and collected into serum tubes with gel (BD Vacutainer®, BD, UK) and tubes with K2EDTA (BD Vacutainer®, BD, UK). Bronchoalveolar lavage fluid (BAL) samples from diseased cattle were sent to virology and microbiology laboratories for agent detection.

### Serum separation

Blood samples taken for serum were kept at room temperature for about 1 h and centrifuged at 20 × g for 10 min (Hettich Rotina 380R®, Hettich, Germany). All serum samples were stored at -20°C until analysis.

### Biomarkers, biochemical and hematological analyses

Blood samples in $K_2$EDTA (BD Vacutainer®, BD, UK) were assessed for total leukocyte count (WBC $\times 10^3/\mu L$) and other hematological parameters using a complete blood count device (VG-MS4e®, Melet Schloesing, France). Complete blood count was measured within 30 min immediately after blood taking. Alanine aminotransferase (ALT), aspartate amino-transferase (AST), gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), total protein (TP), glucose, iron, total bilirubin (Tbil), albumin, creatinine, urea, and creatine kinase (CK) were measured with a fully automatic biochemistry device (Mindray BS120®, Mindray Medical Technology, Istanbul, Turkey) and commercial kits (Mindray Medical Technology, Istanbul, Turkey). Cattle pentraxin-3 (PTX3, Cat: ELK8840, ELK Biotechnology, Wuhan, China) and cattle endothelin-1 (EDN-1, Cat: ELK8839, ELK Biotechnology, Wuhan, China) were measured with ELISA kits. The performance of the kits in terms of sensitivity, detection rate, and specificity for the cattle pentraxin-3 kit were 0.113 ng/ml, 0.32-20 ng/ml, and %94, and for the cattle endothelin-1 kit were 4.74 pg/ml, 15.63-1000 pg/ml, and %92, respectively.

### Glutaraldehyde (GLA) test

The test was performed by mixing 2 ml of blood and 2 ml of 1.4% glutaraldehyde stock solution. The mixture

was put into a 10 ml glass tube. It was turned upside down at 30-second intervals. Coagulation within 15 min was considered positive. Test result; 0-5 min of severe inflammation, 5-10 min of moderate, and 10-15 min of mild inflammation were considered. Coagulation longer than 15 min were considered normal (Turgut, 2000).

## Radiographic imaging

Clinical cases were evaluated in the Radiology Unit of the Department of Surgery, Faculty of CliVeterinary, Kafkas University. Radiological evaluation was performed using 35 × 43 cm cassettes in the right or left L/L position at doses of 80-85 kV and 20-25 mAs, and radiographic images were taken with a CR device (Fujifilm FCR Prima T2 Veterinary Set®, Medical Technology, Turkey).

## Collecting broncho alveolar lavage (BAL) fluid samples

BAL samples were taken from cattle with respiratory system problems included in the study by the method reported by Akyüz *et al*. (2022a), and Ider and Maden (2022). Before the lavage procedure, both nostrils of the cattle were cleaned with alcohol cotton to prevent nasal contamination. After achieving head and neck extension, a disposable sterile naso-gastric tube (4 mm × 1210 mm, Bıçakcılar, Istanbul, Turkey) was advanced transnasal down through the trachea until it encountered slight resistance. Whether the carina area was reached or not was followed up with a repetitive cough reflex. When the carina was reached, the nasogastric tube was withdrawn 1-2 cm, 20 ml of sterile saline (37°C, 0.9% isotonic sodium chloride) was infused into the trachea and immediately aspirated. Approximately 5 ml of the given fluid was withdrawn. One ml of the BAL fluid sample was sent to the microbiology laboratory for bacterial analysis and the remainder to the virology laboratory.

## Virological diagnosis

BAL fluid was taken from cattle with respiratory system problems. The sample was shaked and centrifuged at 20 × g at 4°C for 20 min by a refrigerated centrifuge. For the virological study, the supernatant was taken, passed through a 220 nm filter, and separated into a stock tube.

## Nucleic acid isolation, RT-PCR

A commercial nucleic acid isolation kit (High Pure Viral RNA Kit, Roche, Mannheim, Germany) was used from 50 BAL fluid samples to extract viral nucleic acid. The kit protocol was applied as recommended by the manufacturer. A cDNA synthesis kit (iScript, Biorad) was used to detect RNA viruses. The primers used to detect all agents are listed in Table 1. PCR conditions for BHV-1, pestivirus, BPI-3, and BRSV are as follows: For BHV-1, gB, it was according to Vilcek (1993), PCR reaction was performed under the following conditions in initial denaturation at 94°C for 3 min, 35 cycles of first denaturation at 95°C for 1 min, annealing at 57°C for 1 min, extension at 72°C for 1 min, and final extension at 72°C for 10 min. PCR condition for Pan-pestivirus 5' UTR gene was according to Vilcek *et al*. (1994). PCR reactions were performed under the following conditions: initial denaturation at 94°C for 2 min, 35 cycles of first denaturation at 94°C for 1 min, annealing at 56°C for 1 min, extension at 72°C for 1 min, and final extension at 72°C for 7 min. For BRSV-F genes, the programmes were according to Vilcek *et al*. (1994). PCR reactions were performed under the following conditions: initial denaturation at 94°C for 4 min, 25 cycles of first denaturation at 94°C for 45 s, annealing at 50°C for 45 s, extension at 72°C for 90 s, and final extension at 72°C for 7 min. For BPIV-3-HN genes, the PCR conditions were according to Zhu (2011). PCR reactions were performed under the following conditions: initial denaturation at 93°C for 3 min, 30 cycles of first denaturation at 94°C for 45 s, annealing at 49°C for 45 s, extension at 72°C for 1 min, and final extension at 72°C for 10 min.

## Identification of bacterial agents

BAL fluid samples taken from the cattle were inoculated 50 µL of the sample was spread on blood agar and MacConkey agar to isolate for *Pasteurella multocida* and incubated in an aerobic environment at 37°C for 24-48 h. To isolate *Mycoplasma*, 50 µL sowings were made on *Mycoplasma* agar (20% horse serum, yeast extract, penicillin, and thallium acetate added) and incubated at 37°C for 5-7 days in a microaerobic environment (Ok *et al*., 2019; Van Leenena *et al*., 2020). *P. multocida* was identified by examining the colony morphology,

**Table 1:** Primers used for detection of viral agents in the BRDC group

| Name | | Sequence 5´ → 3´ | Location | Size | Reference |
|---|---|---|---|---|---|
| BoHV-1 gB | F-P1 | CACGGACCTGGTGGACAAGAA | 624-645 | 468 | Vilcek (1993) |
| | R-P2 | CACGGACCTGGTGGACAAGAA | 1091-1070 | | |
| Pan pestivirus | F-p324 | ATGCCCW(A/T)TAGTAGGACTAGCA | 108-128 | 288 | Vilcek *et al*. (1994) |
| | R-p326 | TCAACTCCATGTGCCATGTAC | 395-375 | | |
| BRSV-F gene | F-B1 | AATCAACATGCAGTGCAGTTAG | 114-135 | 711 | Vilcek *et al*. (1994) |
| | R-B2A | TTTGGTCATTCGTTATAGGCAT | 824-803 | | |
| | B3 | GTGCAGTTAGTAGAGGTTATCTTAGT | 126-151 | 481 | |
| | B4A | TAGTTCTTTAGATCAAGTACTTTGCT | 606-581 | | |
| BPIV-3 HN gene | F-HNfwd | GAATGACTCATGATAGAGGTAT | 7221-7242 | 647 | Zhu (2011) |
| | R-Hnseq1 | AGGACAACCAGTTGTATTACAT | 7867-7846 | | |

BRDC: Bovine respiratory disease complex

hemolysis characteristics, Gram stain, oxidase, catalase, indole, and growth on MacConkey agar (Elsayed *et al*., 2021). Sowings on *Mycoplasma* agar were examined every day at ×10 magnification under the microscope for 5-7 days from the third day of incubation. Suspicious colonies were defined as *Mycoplasma* spp. with their ability to grow in inhibitor-free media, typical colony morphologies, and lack of urease activities (Otlu, 1997).

### Statistical analysis

Statistical data were analyzed using SPSS® (SPSS 26.0, Chicago, IL, USA) software. The statistical differences between the groups with normal distribution according to the Shapiro-Wilk test were compared by the independent sample t-test. The obtained results were given as mean ± standard error of the mean (SEM). P<0.05 was considered statistically significant in the evaluation of the results.

## Results

In the physical examination findings in the present study, rectal temperature, respirations per minute, and pulse rates were statistically significantly higher in the BRDC group than those in the control group (P<0.001, Table 2). WBC count was more elevated in the BRDC group compared to the control group (P=0.001, Table 2), while RBC was lower (P=0.001, Table 2). Other complete blood count findings are presented in Table 2.

Gamma-glutamyl transferase (P=0.009, Table 3), urea (P<0.001, Table 3), total bilirubin (P<0.001, Table 3), LDH (P<0.001, Table 3), CK (P<0.001, Table 3), pentraxin-3 (P<0.001, Figs. 1A and B) and endothelin-1 (P<0.001, Figs. 1A and B) levels were statistically higher in the serum of the BRDC group than those in the control group. Glucose (P=0.003), total protein (P<0.001), albumin (P=0.027), and iron (P<0.001) levels were found to be statistically significantly lower in the BRDC group compared to the control group (Table 3). The distribution of viral and bacterial agents in BAL samples of diseased cattle is given in Table 4. In addition, according to the GLA test results of diseased cattle in the BRDC group, 23 had severe inflammation, 14 had moderate inflammation, and 3 had mild inflammation. It was determined that there was no inflammation in the GLA results of the cattle in the control group.

**Table 2:** Physical examination and hematology findings of BRDC and control cattle

| Parameters | BRDC group | Control group | P-value |
|---|---|---|---|
| | Mean±SEM | | |
| Rectal temperature (°C) | 39.05 ± 0.21 | 38.23 ± 0.08 | 0.001 |
| Breaths/min | 38.80 ± 2.65 | 23.60 ± 1.51 | <0.001 |
| Heart beats/min | 105.60 ± 6.58 | 70.80 ± 2.15 | <0.001 |
| Total leukocytes count (×$10^3$/µL) | 21.73 ± 3.44 | 9.28 ± 0.59 | 0.001 |
| Lymphocytes count (%) | 42.10 ± 3.55 | 69.94 ± 1.75 | <0.001 |
| Monocytes count (%) | 3.99 ± 0.34 | 5.80 ± 0.38 | 0.002 |
| Granulocytes count (%) | 53.90 ± 3.47 | 24.18 ± 1.56 | <0.001 |
| Lymphocytes count (×$10^3$/µL) | 11.25 ± 3.09 | 6.53 ± 0.40 | 0.141 |
| Monocytes count (×$10^3$/µL) | 0.62 ± 0.03 | 0.52 ± 0.06 | 0.173 |
| Granulocytes count (×$10^3$/µL) | 9.76 ± 0.82 | 1.98 ± 0.17 | <0.001 |
| Red blood cell count (×$10^6$/µL) | 8.65 ± 0.46 | 10.77 ± 0.38 | 0.001 |
| Mean red cell volume (fL) | 41.05 ± 0.65 | 43.42 ± 0.83 | 0.062 |
| Hematocrit (%) | 34.07 ± 1.63 | 44.12 ± 1.03 | <0.001 |
| Hemoglobin (g/dL) | 10.31 ± 0.51 | 10.43 ± 0.31 | 0.848 |
| Platelet count (×$10^3$/µL) | 341.83 ± 27.45 | 416.70 ± 46.94 | 0.179 |

P<0.05: Indicates statistical significance between BRDC and control groups. SEM: Standard error of mean, and BRDC: Bovine respiratory disease complex

**Table 3:** Some biochemical parameters in the BRDC and control groups

| Parameters | BRDC group | Control group | P-value |
|---|---|---|---|
| | Mean±SEM | | |
| Alanine aminotransferase (IU/L) | 73.49 ± 8.49 | 39.05 ± 5.88 | 0.072 |
| Aspartate aminotransferase (IU/L) | 160.04 ± 31.09 | 131.74 ± 13.01 | 0.609 |
| Gamma glutamyl transferase (IU/L) | 70.81 ± 9.74 | 15.61 ± 1.55 | 0.009 |
| Creatinine (mg/dL) | 1.41 ± 0.17 | 1.54 ± 0.14 | 0.693 |
| Urea (mg/dL) | 73.01 ± 6.05 | 35.48 ± 4.36 | <0.001 |
| Total bilirubin (mg/dL) | 0.19 ± 0.02 | 0.02 ± 0.01 | <0.001 |
| Lactate dehydrogenase (IU/L) | 1085.08 ± 108.31 | 153.82 ± 29.71 | <0.001 |
| Glucose (mg/dL) | 37.80 ± 6.40 | 75.50 ± 9.17 | 0.003 |
| Total protein (g/dL) | 5.68 ± 0.22 | 7.32 ± 0.20 | <0.001 |
| Albumin (g/dL) | 2.68 ± 0.09 | 3.11 ± 0.12 | 0.027 |
| Creatine kinase (IU/L) | 576.45 ± 61.79 | 113.75 ± 18.44 | <0.001 |
| Iron (mg/dL) | 0.60 ± 0.07 | 1.38 ± 0.13 | <0.001 |

P<0.05: Indicates statistical significance between BRDC and control groups. SEM: Standard error of mean, and BRDC: Bovine respiratory disease complex

**Table 4:** Viral and bacterial agents in BAL samples from cattle with BRDC

| Case No. | Viral agents | | | | Bacterial agents | |
|---|---|---|---|---|---|---|
| | Pestivirus | BHV-1 | BRSV | BPI-3 | *P. multocida* | *Mycoplasma* spp. |
| 1 | - | + | - | - | - | - |
| 2 | - | - | - | - | + | - |
| 3 | + | - | - | - | + | - |
| 4 | - | + | - | - | - | - |
| 5 | - | - | - | - | - | + |
| 6 | - | - | - | - | + | - |
| 7 | + | + | - | - | - | - |
| 8 | - | - | + | - | + | - |
| 9 | - | - | - | - | + | - |
| 10 | - | + | - | - | - | - |
| 11 | - | + | - | - | - | - |
| 12 | - | - | - | - | - | - |
| 13 | + | - | - | - | + | - |
| 14 | - | + | - | - | + | - |
| 15 | - | + | - | - | - | - |
| 16 | - | - | - | - | - | - |
| 17 | - | + | - | - | + | - |
| 18 | - | - | - | - | - | + |
| 19 | + | + | - | - | - | - |
| 20 | - | + | - | - | + | - |
| 21 | + | - | - | - | + | - |
| 22 | - | + | - | - | - | - |
| 23 | - | - | + | - | - | - |
| 24 | - | - | - | - | - | + |
| 25 | - | + | - | - | - | - |
| 26 | + | - | - | - | - | - |
| 27 | - | - | - | - | - | + |
| 28 | - | + | - | - | - | - |
| 29 | + | - | - | - | + | - |
| 30 | - | - | - | + | + | - |
| 31 | - | + | - | - | - | - |
| 32 | - | - | - | - | + | - |
| 33 | - | + | - | - | - | - |
| 34 | + | - | - | - | - | - |
| 35 | - | - | - | - | - | - |
| 36 | - | + | - | - | + | - |
| 37 | + | + | - | - | - | - |
| 38 | - | - | - | - | + | + |
| 39 | - | - | + | - | - | - |
| 40 | - | + | - | - | - | - |

+: There is an agent, -: There is no agent, BRDC: Bovine respiratory disease complex, BHV-1: Bovine herpes virus-1, BRSV: Bovine respiratory syncytial virus, and BPI-3: Bovine parainfluenza type 3 virus

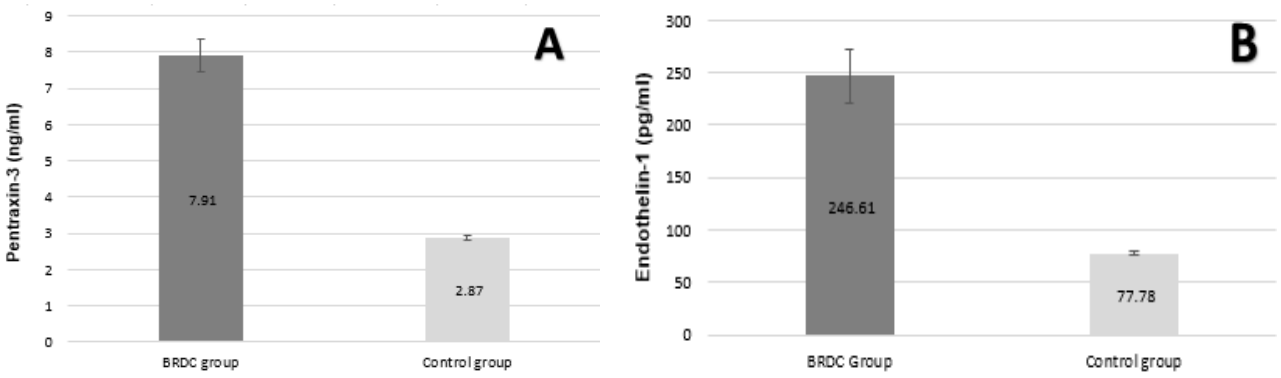


**Fig. 1:** Comparison of mean values of serum pentraxin-3 and endothelin-1 concentrations between BRDC and control groups. (**A**) Comparison of mean serum pentraxin-3 concentration of cattle in BRDC and control groups (P<0.001), and (**B**) Comparison of mean serum endothelin-1 concentration between BRDC and control groups (P<0.001). BRDC: Bovine respiratory disease complex

In radiological examinations of the lungs, a trend in increased radioopacity were observed towrd the cranial lobes. Despite a relative more radiolucency in the caudal lobes, almost all cases showed a clinically severe pneumonia (Fig. 2). RT-PCR image of BHV-1 some positive samples (Fig. 3).

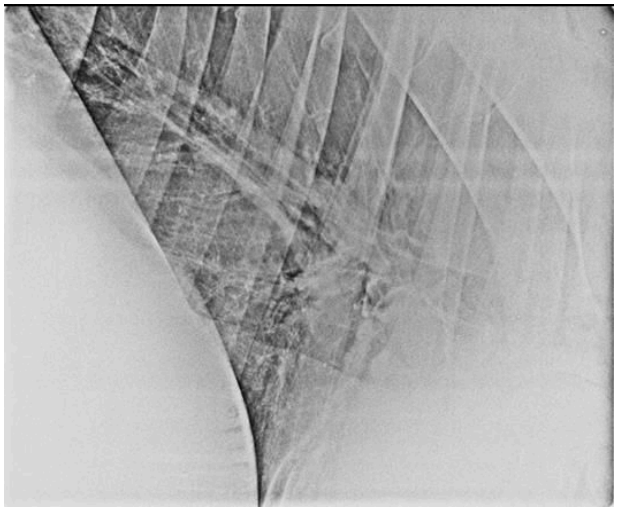

**Fig. 2:** Radiographic image from cattle with BRDC. Radiopaque appearance was dominant in all lung areas. The radiopaque image was observed to become more radiolucent towards the caudal, where the opacity increase was especially in the cranial lobes

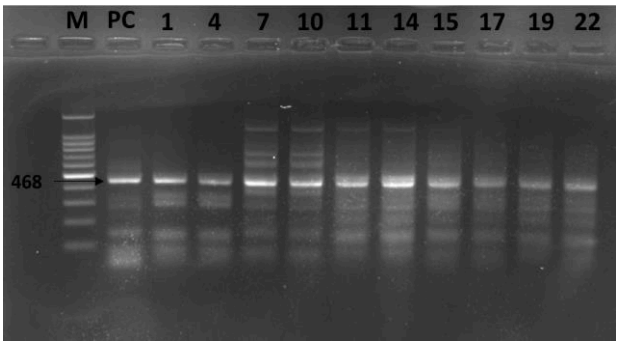


**Fig. 3:** RT-PCR gel electrophoresis of BHV-1 some positive samples. M: Marker, PC: Positive control (468 bp), positive samples; 1, 4, 7, 10, 11, 14, 15, 17, 19, 22

## Discussion

Many viral and bacterial agents are considered the causative agents of the infectious BRDC. BHV1, PI-3, and BRSV are the most common viral agents. Among the pathogenic bacteria causing disease in BRDC, *P. multocida* and *M. bovis* are frequently isolated (Edwards, 2010; Yilmaz and Gokce, 2017). In the present study, these factors were found in the BAL samples of cattle with BRDC.

A study reported that rectal temperature, respiratory, and pulse rates per minute were higher in the BRDC group compared to the control group (Yilmaz and Gokce, 2017). Similarly, in our study, rectal temperature, respiratory, and pulse rates per minute were found to be statistically significantly higher in the BRDC group compared to the control group due to infection. Viral agents can temporarily suppress the immune system of cattle and cause secondary bacterial infections in BRDC (Jones and Chowdhury, 2007). In our study, WBC was statistically significantly higher in the BRDC group than in the control group, which would be due to the secondary bacterial factors accompanying the disease in the BRDC group. The determination of inflammation in the GLA tests in the BRDC group also supports this thought.

A decrease in serum albumin may occur due to degradation due to infections and inflammation (Talkhan *et al*., 2009; Akyüz and Gökce, 2021). In the case of pneumonia, it has been reported that there is a decrease in negative acute-phase protein albumin due to infection-induced inflammation (Bozukluhan *et al*., 2022). In our study, the decresed level of albumin in the BRDC group than in the control group is supposed due to the inflammation caused by viral and bacterial agents. Serum iron levels may decrease in an unbalanced diet, acute or chronic infections, chronic liver diseases, and inflammation (Kaneko *et al*., 2008; Akyüz *et al*., 2022b). In many infections, bactericidal activity increases with decreased serum iron concentration (Akyüz *et al*., 2022b). In our study, infection, anorexia, inflammation, and infective agents were lower in the BRDC group than in the control group.

Pentraxin-3 is an acute-phase protein released from macrophages, dendritic cells, leukocytes, and endothelial cells during the inflammatory response (Libby *et al*., 2009). Acute phase protein levels increase in conditions such as infection, inflammation, trauma, and tissue damage (Petersen *et al*., 2004; Erkılıç *et al*., 2019; Akyüz and Aydın, 2022). In our study, pentraxin-3 levels were statistically significantly higher in the BRDC group than in the control group ($P<0.001$). The reason for this increase may be inflammations and infections caused by viral factors in some cattle in the BRDC group and bacterial factors in others. Additionally, due to damage to various tissues, especially the lung, disease factors triggered the increase in the level of pentraxin-3, an acute phase protein. Pentraxin-3 has an important protective role in bacterial lung inflammation and disease (Townsend and Singh, 2021). Our study determined a high rate of severe inflammation according to the GLA test in cattle with BRDC. This severe inflammation may be due to the lung protection property pentraxin-3, increased in cattle with BRDC.

Endothelin-1 is a very potent vasoconstrictor released by endothelial cells. In endotoxemias, pre-pro-endothelin-1 is released from the heart and lungs, and it increases in direct proportion to the mortality rates of the diseases (Tschaikowsky *et al*., 2000; Shah, 2007; Sonmezer and Tulek, 2015). In our study, the endothelin-1 level was statistically significantly higher in the BRDC group compared to the control group due to damage to the endothelial cells and lung tissue ($P<0.001$). Radiographic examination findings confirm the damage in the lungs. Endothelin-1 is an inflammatory mediator

that may play a key role in both acute and chronic airways, pulmonary circulation, and inflammatory lung diseases (Fagan *et al*., 2001). In our study, there were both acute and chronic cases in the BRDC group. Endothelin-1 may be increased in cattle with BRDC due to severe inflammation. In addition, endothelin-1 may be increased due to the disruption of the airways of cattle with BRDC as a result of possible disease.

In the study, pentraxin-3 and endothelin-1 levels were statistically significantly higher in the BRDC group compared to the control group. As a result, pentraxin-3 and endothelin-1 were found to be diagnostically important in cattle diagnosed with BRDC.

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## Conflict of interest

The authors have declared that no conflicts of interest are associated with this study or its results.

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